REMARKS

1. Claim Status

Claims 39-75 are pending in the application. Claims 39-73 were non-finally rejected in the January 1, 2010 Office Action. Claims 39, 42, 48, 57 and 65 have been amended. Claims 74 and 75 are new. Support for the amendment to the claims can be found throughout the originally filed specification, examples and claims and in particular, on page 2, at the bottom, and page 3 at the top (including in the top text and the first two full paragraphs), page 5, second full paragraph, at page 22, second and third full paragraphs, Tables 1 and 2 on pages 23-24 and on page 24 in the text under table 2 at the bottom of the page for support for the length of the R sidechain. No new matter has been added by way of the present amendment.

Applicant respectfully requests that the claim amendments presented herein be entered in the application as they place the application in a condition for allowance. Applicant maintains for the reasons explained below that claims 39-75 as amended herein are allowable and should be passed to issue. Applicant addresses each of the Examiner's concerns in the sections which are presented hereinbelow.

2. Claims 57-64 Satisfy the Written Description Requirement

In the January 6, 2010 Office Action, the Examiner maintained her rejection of claims 57-64 under 35 U.S.C. § 112,¶ 1 for failure to satisfy written description on grounds that the specification of the application as originally filed, when coupled with the knowledge of those of ordinary skill in the art as of the filing date, did not support a claim to "reducing the likelihood of a recurrence of breast cancer". Applicant traverses these rejections and respectfully maintains that claims 57-64 satisfy written description for the following reasons.

Claim 57 as drafted is directed to a method of reducing the likelihood of a recurrence of breast cancer in a patient. According to the Examiner, the claim entails a treating physician to first determine that the patient would in fact come out of remission absent treatment. Applicants respectfully submit that the Examiner has mischaracterized the claimed method. The limitation in the claimed method is directed to *reducing the likelihood* of a recurrence of breast cancer in a patient and does not imply that a treated patient would necessarily relapse absent treatment. This method is consistent with the current practice for other SERM compounds, in particular, tamoxifen and raloxifene. A recurrence of breast cancer is known to those in the art as is the return of cancer cells to the patient after remission in that patient. As previously explained, those of ordinary skill in the art as of the filing date, knew that the risk of relapse/recurrence of breast cancer implicated such factors as diet, estrogen levels, estrogen metabolites, and the existence of precancerous tissue by biopsy. This is standard practice by those of ordinary skill who treat breast cancer patients and who monitor breast cancer patients in remission. Based on an analysis of such factors, a treating physician could reasonably inhibit or reduce the likelihood of breast cancer relapse or recurrence by simply applying the claimed methods without the need to determine that a relapse was a certainty absent treatment.

The present compounds are characterized as SERMs, and like traditional SERMs such as tamoxifen and raloxifene, have similar activity to, but completely different chemistry from tamoxifen and raloxifene, which are recognized in the art for use in inhibiting the recurrence of breast cancer. The presently claimed steroidal SERMs are used in the same way as tamoxifen and other SERMs. Given the activity of the present compounds as SERMs, and the fact that other SERMs such as taxoxifen, have been used for a number of years before the filing of the present application to reduce the likelihood of breast cancer recurrence in patients, Applicants respectfully submit that the skilled practitioner fully recognizes those individuals for whom this therapy is appropriate and, given that recognition and the convention in the art (vis-à-vis tamoxifen and taloxifene), can use the present compounds within the teachings of the present application consistent with the method of claim 57.

Applicant respectfully submits that the Examiner has misapplied the written description requirement of 35 U.S.C. §112, first paragraph, M.P.E.P. 2163.01 and 2163.02. Pursuant to M.P.E.P. 2163.02, an objective standard for the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed". *In re Gosteli*, 872 F.2d 1008, 1012. Thus, to satisfy the written description requirement, the application as filed must convey to the person of ordinary skill with reasonable clarity that he or she was in possession of the invention and that the invention is whatever is now claimed. In essence, the specification must merely convey that as of the filing date, Applicant was in possession of the invention. It is noted that the description of the invention need not be described literally in order to satisfy the requirement. See M.P.E.P. 2163.02.

In the present application, Applicant clearly provides sufficient description of the invention to convey to those of ordinary skill (a skilled oncologist treating breast cancer patients) that the compounds as claimed could be used in a method to inhibit or reduce the likelihood that breast cancer will recur in a patient. Given the years of experience of practitioners with compounds of similar activity such as tamoxifen and/or ramoxifene in reducing the likelihood of breast cancer recurrence using these SERM agents and the wealth of experience of clinical oncologists in treating breast cancer, a method of using the steroidal SERMs of the present invention to reduce the likelihood of breast cancer recurrence in a patient is fully described and adequately conveyed. This is further supported by the attached declaration of Dr. Richard Hochberg, in paragraph 14.

Accordingly, Applicant maintains that claims 57-64 clearly satisfy the written description requirement and respectfully request the Examiner withdraw her rejection of claims 57-64 on these grounds.

3. **The Rejection of Claims 39, 42, 65, 67, 68 and 70-73 Has Been Withdrawn**

4. Claims 48-51 and 65-73 Satisfy the Written Description Requirement

In the January 6, 2010 Office Action on pages 3-4, the Examiner rejected claims 48-51 and 65-73 under 35 U.S.C. § 112, ¶ 1 for written description. Inasmuch as Applicant has amended claims 48 and 65 and deleted the language to which the Examiner objected, Applicant respectfully submits that the rejection raised by the Examiner has been mooted. This rejection will not be further discussed. It is respectfully submitted that amended claims 48 and 65, and the claims dependent thereon, now satisfy the written description requirement.

5. The Rejection of Claims 57-64 under 35 U.S.C. §112, Second Paragraph Has Been Withdrawn

6. Newly Amended Claims 39-47, 52-56 and 65-73 Satisfy 35 U.S.C. §112, Second Paragraph

The Examiner rejects previously pending claims 39-47, 52-56 and 65-73 under 35 U.S.C. §112, Second Paragraph as being indefinite for the reasons which are stated in the January, 2006 office action on page 4. In response, Applicant has removed the language to which the Examiner objected in independent claims 39 and 65, thus obviated the Examiner's rejection. Applicant respectfully submits that the claims as amended comply with the requirements of 35 U.S.C. §112, Second Paragraph.

7. Claims 39-56 and 65-73 Are Nonobvious Over the Teachings of van den Broek

In the January 6, 2010 Office Action, the Examiner maintained her rejection of claims 39-56 and 65-73 under 35 U.S.C. § 103(a) as being unpatentable for obviousness over U.S. Patent No. 3,972,906 ("*van den Broek*").

According to the Examiner, at the time of the invention of the pending claims, the use of *van den Broek's* estrogenic compounds to treat menopausal symptoms and breast cancer would have been obvious. Essentially, the Examiner argues that "the issue is not whether the art recognized the differences in the action of the compounds in different target organs. The issue is whether the art teaches or suggests the use of the compounds as claimed by the instant invention."

Applicant agrees with the Examiner in the characterization of the issue of obviousness/non-obviousness to be resolved, but further points out that the issue is clarified by requiring that the same or similar results need be obtained. However, Applicant respectfully contends that the compounds as claimed evidence unexpected activity as selective estrogen receptor modulators (SERMs) and this unexpected activity, which was completely unrecognized by van den Broek, has given risen to unexpected results for the amended claimed methods which are clearly patentable and distinguishable over the teachings of van den Broek, which issued in 1976[1].

Applicant's claimed methods represent the first use of steroidal SERM's:
(a) to treat menopausal symptoms in a patient while reducing the risk that the patient develops, or experiences a recurrence of, an estrogen-sensitive cancer;
(b) to treat an estrogen-sensitive cancer; and
(c) to reduce the likelihood of a reoccurrence of breast cancer in a patient.

At the time of the invention of the pending claims, the non-steroidal SERM Tamoxifen® was indicated for the treatment and prevention of breast cancer. It was recognized that post-menopausal patients treated with Tamoxifen® could benefit from a potential reduction in bone loss and cholesterol levels. Also, at the time of the invention of the pending claims, the use of steroidal estrogen receptor agonists such as those

[1] Applicant points out the issue date of van den Brock only to emphasize the point that if van den Broek had taught or suggested the present invention as the Examiner argues, surely one of ordinary skill would have discovered the highly desirable SERM activity of the putatively disclosed compounds of van den Broek well before Applicant's invention in 2002, some *twenty-six* years later.

disclosed by the art of record (van den Broek) to treat post-menopausal symptoms were associated with an enhanced risk of breast cancer in that therapy. The present invention addresses the concerns of the art with the steroidal compounds of the present invention which exhibit unexpected SERM activity.

Applicant respectfully submits that van den Broek does not teach or suggest that *any* of the compounds which are disclosed therein exhibit selective estrogen receptor modulator (SERM) activity as in the present invention. Instead, van den Broek teaches a myriad number of compounds which exhibit a broad range of activities which include contraceptive, estrogenic, progestational, ovulation-inhibiting, gonad-inhibiting and anabolic properties. Van den Brock is primarily directed to chemical compounds and the disclosure set forth in that reference is almost exclusively devoted to chemical compounds and chemical synthesis of those compounds. There is no biological activity of *any* of the compounds exemplified in van den Broek. ***None.***

With respect to the suggested estrogenic activities of the van den Broek compounds, the only activity disclosed or suggested therein which is even relevant to the patentability of the present invention appears in column 2, lines 28-48, where van den Broek discloses that certain 11β-substituted steroidal compounds exhibit estrogenic (agonist) properties. In particular, van den Broek cites a number of specific compounds with different pharmacophores as exhibiting estrogenic activity. However, the ***only*** specifically disclosed compounds relevant to the present invention and having a similar estradiol pharmacophore to those used in the present invention are 11*β*-methoxymethyl-ethinyl-estradiol and 11*β*-chloromethyl-ethinyl-estradiol. These estradiol compounds of van den Broek have a methoxymethyl group or a chloromethyl group at the 11β position of estradiol and an ethinyl group at the 17 position of estradiol. See, van den Broek, column 2, lines 28-48. It is noted that every compound which is *specifically* disclosed by van den Broek as having estrogenic (agonist) activity has a *short-chain group* at the 11β position of the steroidal pharmacophore, i.e., a chain-length of 3 (methoxymethyl) or 2

(chloromethyl) non-hydrogen atoms, regardless of pharmacophore. None of the other compounds is specifically disclosed in van den Broek as having estrogenic activity.

The biological activity (estrogen agonist activity) suggested in van den Broek for the disclosed short-chain 11β substituents (methoxymethyl or chloromethyl) is corroborated by the experiments presented on pages 22-25 of the present application. Indeed, a review of the structure activity relationship related to 11β substituents of estradiol in the present application (see especially tables 1 and 2 on pages 23 and 24) evidences that the short-chain compounds which are *specifically* disclosed by van den Broek do *indeed* exhibit estrogenic activity, but when the 11β side-chain is lengthened to 5 or more non-hydrogen atoms as presently claimed, the compounds become ***anti***-estrogenic, an unexpected result, and a result which stands in complete contrast to the biological activity of the compounds disclosed by van den Broek. The compounds of the present invention exhibit *anti-estrogenic* activity consistent with their activity as SERMS, not estrogen agonists, as taught and required by van den Broek. Van den Broek does not disclose or suggest the pharmacological activity (SERM) of the presently claimed compounds. Given the deficiency of van den Broek, van den Broek clearly does not disclose or suggest the methods of the present invention which rely on the SERM activity of the claimed compounds in order to practice the claimed method, completely distinguishable from the prior art teachings.

It is respectfully submitted that the estrogenic compounds which are disclosed by van den Broek are contraindicated for use in the presently claimed methods. For example, each of the methods which are presented in independent claims 39, 48, 57 and 65 rely on the unexpected SERM activity of the claimed compounds in order to effectively and favorably practice the claimed invention. Noting that estrogen agonists are *contraindicated* in patients with or at risk for estrogen-sensitive cancer such as breast cancer, and estrogen agonists *worsen*, rather than *treat*, these cancers, the present compounds, which are anti-estrogenic in those tissues where estrogen-sensitive cancers

develop, provide meaningful utility and benefit in the methods of the present invention. The compounds of van den Broek do not.

The presently pending claims make use of the unexpected activity exhibited by the claimed compounds. Thus, in claim 39, which is directed to a method for treating menopause while reducing the risk that a patient will develop an estrogen-sensitive cancer, the SERM compounds as claimed are particularly useful because they are effective against estrogen-sensitive cancer, whereas the van den Broek estrogenic compounds are *contraindicated* because estrogen agonists actually *increase* the risk of estrogen-sensitive cancers. In claim 48, which is directed to treating an estrogen-sensitive cancer in a patient, treatment is favorably provided by the SERM compounds of the present application, whereas the van den Broek estrogenic compounds are *contraindicated* (see the discussion below and the attached declaration of Dr. Richard Hochberg, in paragraph 12). In claim 57, which is directed to reducing the likelihood of a recurrence of breast cancer (an estrogen-sensitive cancer), the compounds of the present invention, because of their unexpected SERM activity, find favorable use, whereas, the van den Brock estrogen compounds are again *contraindicated.* Likewise, in claim 65, which is directed to a method for treating menopause in a patient with an estrogen-sensitive cancer, the compounds according to the present invention exhibit favorable activity in treating the symptomology of menopause without exacerbating estrogen-sensitive cancers (because they are estrogen *antagonists* in estrogen-sensitive tissues), whereas the van den Broek compounds are contraindicted for the method of claim 65 because of the disclosed estrogenic agonist activity, which exacerbates and is contraindicated in estrogen-sensitive cancer. The same is true for all of the remaining claims, which are dependent on claims 39, 48, 57 and 65.

In short, the presently claimed methods deviate from the prior art precisely at the point of invention where the present invention is favorably used because of the unexpected biological activity (SERM) exhibited by the claimed compounds, whereas the compounds of the prior art are actually contraindicated. The Examiner's argument that

the compounds disclosed by van den Broek would *inherently* produce the claimed methods is not credible, given that the compounds which are claimed in the present methods are *not* specifically disclosed by van den Brock, and if one were to *theoretically* make compounds according to the present invention and test those compounds in a traditional estrogen assay (see the previously submitted May 2, 2007 declaration of Richard Hochberg, in particular at paragraph 19), the person of ordinary skill would have realized that the compounds had no art recognized estrogen agonist activity. The person of ordinary skill would have concluded that the presently claimed compounds, in essence, are essentially *useless* for the purposes for which estrogen agonist compounds are taught in van den Broek.

Applicants further submit that the presently claimed compounds having SERM activity are not taught by van den Broek and one of ordinary skill would not have been motivated to make and use the present compounds in the presently claimed methods which rely on SERM activity, given the teachings of van den Broek. Applicants respectfully submit that the compounds according to the present invention, which exhibit anti-estrogenic activity in traditional estrogen receptor models (see paragraphs 14-22 of the previously submitted declaration of Dr. Richard Hochberg dated May 2, 2007, enclosed) would not have been considered useful by van den Broek for treating menopause, because menopause treatment traditionally required estrogen agonist activity in the vagina and uterus, to address vaginal dryness and hot flushes, whereas the present compounds, are anti-estrogenic in the vagina and uterus. Thus, the unexpected SERM activity which is exhibited by the present compounds stands in complete contrast to the desired activity (estrogenic agonist) of van den Broek and would not be considered appropropriate. Moreover, van den Broek does not disclose SERM activity of any of the disclosed compounds. It is certainly not obvious to use a compound whose activity is not known in a method which requires that activity.

Based on what was known in the prior art and their own knowledge, those of ordinary skill in the art at the time of the invention of the pending claims would have

reasonably believed that the presently claimed SERM compounds would have failed to achieve the purposes of the van den Broek taught methods *and* separately, the purpose for which the currently claimed methods are applied, precisely because of the unknown and unexpected (SERM) activity exhibited by the presently claimed compounds. *See Takeda Chem. Indust. v. Alpharma Pty Ltd.*, 492 F.3d 1350; 2007 U.S. App. LEXIS 15349; 83 U.S.P.Q.2D (BNA) 1169 (Fed. Cir. 2007), *cert. denied*, 2008 U.S. LEXIS 3015 (U.S., Mar. 31, 2008).

Regarding the Examiner's arguments that a compound and its properties are not separable, Applicants merely point out that while that basic tenet is true, the actual compounds used in the present invention exhibit substantially different and unexpected pharmacological activity from the compounds taught by van den Broek and the methods of the present invention make use of these activity differences between the compounds used in the present invention and the prior art taught compounds. While it is true that one cannot separate a compound from its properties, where, as here, the properties of the compounds deviate from the teachings of the prior art and Applicant makes (new) use of those properties in a way that clearly relies on and distinguishes that unexpected activity from the teachings of the prior art, invention exists.

It is Applicant's further respectful position that the Examiner's obviousness rejection ignores both the purposes for which the claimed methods are administered and the advantages of those methods, and further presupposes knowledge on the part of skilled artisans about the nature and properties of the administered compounds that could have only been gained from Applicant's invention. Van den Boerk clearly did not disclose SERM activity for any disclosed compound, let alone compounds used in the present invention. Such a hindsight reconstruction of the prior art is legally impermissible. *See Ortho-McNeil Pharma., Inc. v. Mylan Labs, Inc.*, 520 F.3d 1358, 86 U.S.P.Q.2d 1196 (Fed. Cir. 2008) (*KSR* posits a situation with a finite, and in the context of the art, small or easily traversed, number of options that would convince an ordinarily skilled artisan of obviousness; only by impermissible hindsight could patentee's selection

and modification of a compound putatively developed for a different application be found obvious in this instance).

Accordingly, Applicant maintains that claims 39-56 and 65-73 are nonobvious over van den Broek.

8. Claims 39-56 and 65-73 Are Nonobvious Over the Teachings of van den Broek, in view of Cameron, Palkowitz and Bodor

The Examiner has rejected claims 39-56 and 65-73 under 35 U.S.C. §102(a) as being unpatentable over van den Broek, in view of Cameron, U.S. patent publication no. 2001/0025051 ("Cameron"), Palkowitz, U.S. patent no. 6,268,361 ("Palkowitz") and Bodor, et al., U.S. patent no. 4,617,298 ("Bodor") for the reasons which are set forth in the January, 2010 office action on pages 6-8. Essentially, the Examiner argues that because estrogen was known to be used to treat "estrogen-sensitive" cancer, as well as the symptoms of menopause, it would have been obvious to the skilled artisan to treat estrogen-deficiency syndromes such as menopausal symptoms, osteoporosis and estrogen-dependent cancer using the compounds as taught by van den Broek. The Examiner further argues that the treatment which is taught by van den Broek, inherently results in the presently claimed methods. Applicants respectfully traverse the Examiner's rejection for the following reasons.

The teachings of van den Broek and the failure of the prior art to recognize the existence of SERM activity in any of the compounds disclosed therein, or the benefits that SERM activity provides in relationship to the claimed methods, discussed in detail hereinabove, is referenced here. In essence, van den Broek failed to teach the unexpected pharmacological activity of the presently claimed compounds which are used in methods according to the present invention, and the known pharmacological activity as taught by Broek is *contraindicated* for use in the presently claimed methods. It is the clearly distinguishable and unexpected SERM activity of the compounds as presently claimed in

methods which rely on and distinguish over the prior art estrogenic compounds based upon that unexpected activity which forms the basis and foundation of the patentability of the present invention.

Van den Broek does not disclose or suggest the present invention for the reasons which are presented hereinabove. None of Cameron, Palkowitz or Bodor, taken alone or in any combination, cures the deficiencies of van den Broek in failing to suggest the present invention. Much of the disclosure of Cameron, Palkowitz and/or Bodor is actually irrelevant to the present invention, because the claimed compounds and pharmacophores disclosed in each of those references are simply unrelated to the present invention. The more generic disclosure of those references upon which the Examiner relies, as to the use of estrogen agonists in the treatment of estrogen-sensitive cancers, actually *supports* the non-obviousness and patentability of the present invention, rather than rendering the present invention obvious.

Cameron is directed to certain compounds for preventing breast cancer. These compounds, which are completely unrelated structurally to the present invention, are said to be useful for preventing breast cancer. The teachings of Cameron have little to do with the present invention other than to point out that estrogen agonists have been used in combination with other agents in the treatment of *prostatic* cancer (paragraph 003), which is an androgen sensitive cancer, and are *contraindicated* for use in the treatment of estrogen-sensitive cancers, including breast and endometrial cancer (paragraph 008). Notwithstanding the Examiner's reliance on the teachings of Cameron, those teachings actually emphasize the patentability of the present invention and support Applicant's point- that compounds which have SERM activity (those used in the present invention) are favorably used in the present methods, whereas the prior art estrogen agonist compounds (such as those taught by van den Broek) are actually contraindicated for use in the present invention. Cameron teaches the person of ordinary skill to avoid estrogen agonists and to favorably use SERMS in breast cancer and uterine cancer, the precise support for patentability that Applicant relies on. However, Cameron suggests nothing

with respect to any compound disclosed in van den Broek or any steroidal compound for that matter, and no such conclusion or inference could be drawn. Cameron, contrary to rendering the present invention obvious, actually *supports* the patentability of the present invention.

Turning to the teachings of Palkowitz, this reference is relevant in that it, like Cameron, also teaches that the use of estrogen agonists in treating estrogen-sensitive (estrogen-dependent) cancers is contraindicated and to be avoided (column 2, lines 40-57). Palkowitz is otherwise related to naphthyl compounds which are completely unrelated to the chemical structures of the compounds used in the present invention. Just as Cameron could be seen by one of ordinary skill in the art as supporting Applicant's claim for patentability, rather than the Examiner's position, so too does Palkowitz support Applicant's invention. In short, Palkowitz does nothing to obviate the deficiencies of the teachings of van den Broek and Cameron in failing to suggest the present invention.

Regarding the teachings of Bodor, this reference is directed to a number of compounds which are principally directed to certain salts of steroids having estrogenic activity which are used to enhance weight control activity. None of the compounds which are disclosed therein are related to the present invention and none of the compounds disclosed therein or the disclosure provided, even allude to the compounds and methods of the present invention. Bodor, in the background of the invention section, does make an oblique reference to the use of estrogen compounds in the treatment of breast cancer, but otherwise does not provide any disclosure which is even relevant to the present invention. It is noted that estrogen agonists actually are contraindicated for use in the treatment of estrogen-sensitive cancers (see the attached declaration of Dr. Richard Hochberg), and although estrogen agonists historically have been used in combination with other agents to treat cancer, that approach has been discontinued because of the tendency of that therapy to exacerbate or worsen the estrogen-sensitive cancer. Thus, the much earlier published Bodor must also be read in conjunction with the more contemporary Cameron and Palkowitz as supporting the relevance and benefit of the

present invention. Bodor, in essence, does essentially nothing to cure the deficiencies of the other art in failing to suggest the present invention.

Note that with respect to the present invention, the compounds which are presently claimed in the methods of present invention do not exhibit favorable activity as estrogen agonists and are otherwise known as anti-estrogens. So, even if Bodor's 1986 disclosure is read in isolation (i.e., without reference to the later published Cameron and/or Palkowitz) in combination with van den Broek, and estrogen agonists are suggested for treating breast cancer (an approach which is actually counterproductive and deleterious to the breast cancer therapy outcome- see the attached declaration of Richard Hochberg), the present compounds would not be used in those teachings because, as explained hereinabove, the present compounds *do not* exhibit estrogen agonist activity as called for by the Bodor treatment.

The position of the Examiner that it would have been obvious to use the presently claimed SERM compounds for the treatment of estrogen-dependent cancer because the prior art teachings suggest the use of the van den Broek estrogen agonist compounds for the treatment of estrogen-sensitive cancers as taught by Cameron, Palkowitz and Bodor is simply not credible. As discussed above, the person of ordinary skill would not have recognized, from van den Broek, the SERM activity of the present invention, which is favorably used in the present invention. Whether one relies on the sole teachings of Bodor or the combined teachings of Bodor with either or both of Cameron and Palkowitz, one is left with the view that the disclosed compounds of van den Broek are not to be used in the present invention. In this sense, the prior art actually *teaches away* from the present invention. The person of ordinary skill would not have used the presently claimed compounds in methods requiring estrogenic agonist activity (Bodor) because the anti-estrogenic activity of the presently claimed compounds is actually *inconsistent* with the requirement for estrogenic agonist activity as taught by van den Broek and Bodor (despite the fact that the suggested method was later shown to be ineffective and/or deleterious). If one were to rely on Cameron and Palkowitz, alone or in combination

with Bodor, these references would not cure the deficiencies of van den Broek- they would actually point out the fallacy and inadequacy of using the van den Broek disclosed compounds to treat estrogen sensitive cancer as taught by Bodor. In either instance, if analyzed correctly, one of ordinary skill would not have recognized the SERM activity of the presently claimed compounds because that activity was not even obliquely mentioned by van den Broek, or any of Cameron, Palkowitz and/or Bodor. It was not until the present application that the SERM activity of the presently claimed compounds became known and the benefit of such activity in the methods of the present invention would have been realized.

As a separate note, contrary to the Examiner's contention, the presently claimed invention is not inherent to the disclosure of the prior art references, because, as explained, the person of ordinary skill would not have even used the presently claimed compounds because they were not suggested for use as SERMS and would not have the requisite activity (as estrogen agonists) as taught by van den Broek. The Examiner's reliance on the doctrine of inherency here is not cogent inasmuch as the doctrine of inherency requires the inevitability of the claimed method occurring as a consequence of practicing the invention which is disclosed and there is no disclosure in van den Broek or in any of Cameron, Palkowitz and/or Bodor which inevitably points to the use of the presently claimed compounds in the present methods. The use of the specifically disclosed estrogen agonist compounds of van den Broek, required by a cogent inherency analysis, would clearly not result in the present invention. Contrary to the Examiner's position, Applicant has not merely identified or even used inherent aspects of methods of treatment disclosed or otherwise suggested by *van den Broek* or the other references. In particular, using unidentified synthetic steroids possessing SERM activity for the purposes for which Applicant's claimed methods are administered was not suggested by, and in fact was contrary to, the teachings of the art.

Indeed, the present methods are not even accidentally practiced by relying on the teachings of the prior art given that van den Broek and Bodor teach the requirement for

estrogen agonist activity (which the presently claimed SERM compounds do not possess) and the remaining teachings of Cameron and Palkowitz teach that the use of estrogen agonists should not even be used in the first place. The Examiner's reliance on the doctrine of inherency here is respectfully, misplaced. *Cf. Rapoport v. Dement, et al.*, 254 F.3d 1053, 1059, 59 U.S.P.Q. 2d 1215 (Fed. Cir. 2001).

It is respectfully submitted that the presently claimed invention is patentable. The unexpected activity of the claimed compounds as SERMS is neither disclosed nor suggested by the art of record and this unexpected activity has been put to use in claimed methods which clearly rely on and distinguish over the art based upon this unexpected activity.

Given what was known in the prior art and their own knowledge, those of ordinary skill in the art at the time of the invention of the pending claims in the present methods would have reasonably believed that the presently claimed compounds would have failed to achieve the purposes of the prior art taught methods *and* the purpose for which the currently claimed methods are applied. *See Takeda Chem. Indust. v. Alpharma Pty Ltd.*, 492 F.3d 1350; 2007 U.S. App. LEXIS 15349; 83 U.S.P.Q.2D (BNA) 1169 (Fed. Cir. 2007), *cert. denied*, 2008 U.S. LEXIS 3015 (U.S., Mar. 31, 2008). The present invention is clearly patentable over the disclosed prior art.

For the above reasons, Applicants respectfully assert that the claims set forth in the amendment to the application of the present invention are now in compliance with 35 U.S.C. Applicants respectfully submit that the present application is now in condition for allowance and such action is earnestly solicited.

No fee is due for the presentation of the amendments made herein. A petition for an extension of time is enclosed as is authorization to debit Deposit Account 04-0838. Please charge any additional fee due or credit any overpayment to Deposit Account No. 04-0838.

If the Examiner believes that discussing the present application with the undersigned attorney may materially advance the prosecution of this application, She is cordially requested to telephone the undersigned at the telephone number listed below.

Respectfully submitted,

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CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that this correspondence is being sent by facsimile transmission to Examiner Barbara Badio in Group Art Unit 1628 of the United States Patent and Trademark Office, at P.O. Box 1450 Alexandria, Virginia 22313-1450" on June 10, 2010.

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Henry D. Coleman